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(54) Abstract Title
Compositions comprising trehalose for forming tablets

(57) A sugar composition for tableting by direct compression comprises a minor fraction, preferably 10-35%, of particulate trehalose in combination with a major fraction of one or more substances, such as sugars other than trehalose, that are not directly compressible to form tablets having high integrity. The tablets may be used as a confectionary item or as a drug. The sugar may be one or more of sucrose, glucose (dextrose), fructose, lactose, maltose and sugar alcohols but is preferably sucrose. Preferably the one or more sugars other than trehalose make up from 50-98 % of the composition and in combination with trehalose make up at least 90% of the composition. The composition is preferably free of binders or granulating agents but may comprise 0.1-10% of a flavouring agent, such as a non-sugar sweetener, and/or comprise 0.1-10% of a medicinal substance. A preferred method of manufacture of the sugar composition comprises spray drying of the constituents or coating trehalose onto the major constituents followed by compression at 40-200 Mpa to give tablets with a crushing strength of at least 2 Kp (Kg force).

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WO97/28788 describes tablets comprising a major fraction of trehalose as a diluent or excipient. The resulting tablets can be used as vehicles for oral administration of therapeutic substances. The tablets may be produced by direct compression. However, there is no suggestion that a minor fraction of particulate trehalose could be used to confer direct compressibility on sucrose or other substances that are not directly compressible.

Accordingly, the present invention provides a sugar composition for tableting by direct compression, comprising a minor fraction of particulate trehalose in combination with a major fraction of one or more substances that are not in themselves sufficiently directly compressible to form tablets having high integrity.

The minor fraction of particulate trehalose is preferably from 2% to 50% by weight of particulate trehalose based on the weight of the composition, more preferably from 5% to 40% by weight of particulate trehalose, still more preferably from 10% to 35% by weight of particulate trehalose, and most preferably from 15% to 30% by weight of particulate trehalose.

The particulate trehalose may have any particle size in the ranges conventionally used for tableting. Typically, the particulate trehalose is a powdered trehalose. Preferably, the trehalose is substantially free of water other than water of crystallisation.

The particulate trehalose may be an amorphous, i.e. substantially non-crystalline as determined by X-ray diffraction. Amorphous trehalose can be formed, for example, by spray drying of an aqueous solution of trehalose, or by spinning trehalose in a candy floss type of machine.

The particulate trehalose may in the alternative be crystalline. The crystalline trehalose may be anhydrous, or may comprise water of crystallisation,

invention provides pharmaceutical tablets that consist mainly of the a pharmaceutical active ingredient with only a small amount of excipients. Preferably , such tablets contain at least 50%, preferably at least 60% by weight of the pharmaceutically active ingredients. A minor fraction of trehalose in such tablet compositions can greatly improve the properties of tablets obtained by direct compression.

Preferably, the major fraction comprises one or more sugars other than trehalose, and more preferably the major fraction comprises at least 50%, more preferably 75% and most preferably at least 90% by weight based on the weight of the minor fraction of one or more sugars other than trehalose. Preferably, the one or more sugars are selected from the groups consisting of sucrose, glucose (dextrose), fructose, maltose, lactose, sugar alcohols such as inositol or sorbitol, and mixtures thereof. Preferably, the sugars comprise one or more powdered (icing) sugars, and more preferably the sugars consist essentially of powdered sugars.

It is a particular advantage of the present invention that the particulate trehalose can be used to achieve tableting by direct compression of particulate sucrose products that are otherwise not directly compressible to form tablets having high integrity.

Preferably, the major fraction makes up from 50% to 98%, preferably from 60% to 90%, more preferably from 65% to 85% of the sugar composition according to the present invention. Preferably, at least 90% by weight of the composition is made up of trehalose and one or more other sugars that are not directly compressible as hereinbefore defined, preferably sucrose. Most preferably, the composition consists essentially of trehalose and one or more other sugars that are not directly compressible as hereinbefore defined, preferably sucrose.

The sugar compositions according to the present invention are especially suitable for the manufacture of sweets, such as mints, by direct compression.

coating a minor fraction of trehalose onto particles of a major fraction of one or more substances that are not suitable for tableting by direct compression.

The coating may, for example, be achieved by applying an aqueous solution of trehalose to the solid particles of the major fraction with stirring, followed by drying. Alternatively, the solid particles of the major fraction could be moistened, and then admixed with powdered trehalose. Preferably, the coating process takes place in a spray drier or fluidised bed, in which an aqueous solution of trehalose, or trehalose plus sugar or other non-directly compressible material, is sprayed onto particles of the major fraction and then dries on them to form a coating.

The present invention further provides a method of manufacture of a tablet comprising the steps of: providing a sugar composition according to the present invention; followed by directly compressing the sugar composition to form the tablet. The method preferably does not include any granulation step. Preferably, the sugar composition is substantially free of binders or granulating agents. Preferably, the step of direct compressing is carried out at a pressure of from 40 MPa to 200 MPa.

Finally, the present invention provides a directly compressed tablet comprising a minor fraction of trehalose, wherein the tablet is obtainable by a method according to the present invention.

Preferably, the tablet according to the present invention has a hardness, as determined by the method hereinafter described as Procedure 1, of at least 2 kiloponds (Kp), preferably at least 5 Kp, and more preferably at least 10 Kp.

Preferably, the tablet according to the present invention has a fracture strength, as determined for a tablet of diameter 16mm and thickness 3mm by the method hereinafter described as Procedure 2, of at least 1000 g, preferably at least 2000 g and most preferably at least 2500 g.

A tableting composition was made up as described in Example 1, but with the components in the following proportions: 19.7% spray dried trehalose, 78.8% sucrose, 1% magnesium stearate, and 0.5% mint flavour. The composition was then pressed into tablets as described in Example 2.

The resulting tablets had excellent integrity and hardness. The appearance and sensory attributes of the tablets were typical of those desired for confectionery mints.

Example 4

An alternative method of preparing directly compressible tableting compositions was performed as follows.

Trehalose dihydrtae (30% w/w as anhydrous) and sucrose (70% w/w) were dissolved in deionised water to obtain 52% w/w solids at 40°C. The solution was spray dried using an inlet temperature of 215°C and an outlet temperature of 115°C. Sucrose was fed to the top of the tower around the spray nozzles so that it was coated with the trehalose/sucrose blend to give a final tableting composition of 20% w/w trehalose and 80% w/w sucrose.

Example 5

The tableting composition of Example 4 was compressed to form tablets as described in Example 2. The resulting tablets were similar to those obtained in Example 2.

Example 6 (comparative)

A comparative experiment was carried out to sudy the tableting of sucrose by direct compression.

Comparative compositions were made up consisting of 99% w/w powdered sucrose with 1% w/w magnesium stearate, and 99% w/w particulate crystalline sucrose with 1% w/w magnesium stearate. Attempts were then made to tablet these compositions by direct compression as described in Example 2.

A peak positive force (the total force required to break the tablet) is calculated in grams.

The tablets made from compositions according to the present invention had fracture strengths of 1000g or more up to 3000g or more. The comparative tablets of Example 6 had fracture strengths much less than 1000g.

The above embodiments have been described by way of example only. Many other embodiments falling within the scope of the accompanying claims will be apparent to the skilled reader.

9. A sugar composition according to any of claims 3 to 8, wherein said one or more sugars other than trehalose are powdered sugars.

10. A sugar composition according to any one of claims 1 to 9, further comprising from 0.1 to 10% w/w of a flavouring agent.

11. A sugar composition according to claim 10, wherein said flavouring agent comprises a non-sugar sweetener.

12. A sugar composition according to any one of claims 1 to 7, further comprising from 0.1 to 10% w/w of a medicinal substance.

13. A method of manufacture of a sugar composition, said method comprising providing an aqueous solution or dispersion of trehalose and one or more substances, followed by spray-drying the aqueous solution or dispersion to provide a sugar composition according to any one of claims 1 to 12.

14. A method of manufacture of a sugar composition, said method comprising coating trehalose onto particles of one or more substances that are not suitable for tableting by direct compression, to provide a sugar composition according to any one of claims 1 to 12.

15. A method of manufacture of a tablet comprising the steps of: providing a sugar composition according to any one of claims 1 to 12; followed by directly compressing the sugar composition to form said tablet.

16. A method of manufacture of tablet according to claim 15, wherein said sugar composition is substantially free of binders or granulating agents.

17. A method of manufacture of a tablet according to claim 15 or 16, wherein said step of directly compressing is carried out at a pressure of 40MPa to 200MPa.

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Search Report under Section 17

Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

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Other: Online: CAS-ONLINE, EPODOC, JAPIO, TXTUS1, TXTUS2, TXTEP1, TXTGB1, TXTWO1, WPI

Documents considered to be relevant:

Category	Identity of document and relevant passage		Relevant to claims
X	EP 0882408 A1	(HAYASHIBARA) see especially claim 1 and examples A-2 and B-1	1-11, 14-20
X	EP 0788791 A1	(OTSUKA) see especially page 1, lines 19-27 and page 4, lines 47-54	1-5,9-12, 15-20
X	WO 98/05305 A1	(QUADRANT) see especially page 2, lines 10-12, page 3, lines 11-16, page 5, lines 5-7 and examples	1-3,9-12, 15,17-20
X	US 4762857	(BOLLIN) see especially col 4, lines 28-63	1,12,13, 15-20

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
&	Member of the same patent family	E	Patent document published on or after, but with priority date earlier than, the filing date of this application.